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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/091,608	05/17/1999	CHRISTOPHER ROBERT BEBBINGTON	48418	5129

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EXAMINER
WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 06/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/091,608	Applicant(s) BEBBINGTON ET AL.	
	Examiner Joseph Woitach	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1 136(a) In no event however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U S C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment See 37 CFR 1 704(b)

Status

1)☒ Responsive to communication(s) filed on *10 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,21-24,28-31,33-42,46,47 and 53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,21-24,28-31,33-42,46,47 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 May 1999* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s) _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continued Prosecution Application

The request filed on December 10, 2001, paper number 15, for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/091,608 is acceptable and a CPA has been established. An action on the CPA follows.

DETAILED ACTION

Please note that the Examiner of record and art unit has changed. The Examiner of record is now **Joseph T. Woitach** and the group art unit is now **1632**.

This application is a 371 National stage filing of PCT/GB/03209, filed December 23, 1996.

Applicants' amendment filed December 10, 2001, paper number 16 has been received and entered. Claims 14, 20, 25, 26, 27, 50 and 51 have been canceled. Claims 11, 21-24, 28-31, 33-36, 38-42, 46 and 47 have been amended. Claim 53 has been added. Pleas note that the numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims

previously presented (whether entered or not). Misnumbered claim 52 been renumbered 53. Claims 11, 21-24, 28-31, 33-42, 46, 47, and 53 are pending and currently under examination.

Claim Objections

Claim 36 objected to because of informalities is withdrawn.

The amendment to the claim has obviated the basis of the rejection.

Claims 11 and 31 are objected to because of the following informalities, specifically:

With respect to claim 11, as generally supported in the present disclosure CDR is the acronym of complementarity determining region. When not specifically defined in the specification, the first presentation of an abbreviated term should be denoted by setting forth the full name indicating the term to be used subsequently.

With respect to claim 31, because claim 52 has been renumbered claim 53, claim 31 should be amended to reflect this change. Otherwise, claim 31 is dependent on a canceled claim.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11, 21-24, 28-31, 33-42, 46 and 47 rejected under 35 U.S.C. 112, first paragraph, for the reasons of record as based on a disclosure which is not enabling is withdrawn.

Claims 11, 21-24, 28-31, 33-42, 46 and 47 rejected under 35 U.S.C. 112, first paragraph, for the reasons of record, because the specification, while being enabling for use in cultured cells of the embodiments recited in Examples 2-6 of the specification (pp. 24-36), does not reasonably provide enablement for the broad range of embodiments embraced by the instant claims is withdrawn.

Amendments to the claims have obviated the basis of the rejections. Additionally, it is noted that the present claims are directed to products with intended uses both *in vitro* and *in vivo*. The previous office action set forth many barriers to gene therapy protocols recognized in the art, however as noted in the basis of the rejection, the present disclosure demonstrates that the delivery system can be used and can be effective for use in cells in culture. Providing one enabled use for the instantly claimed product, Applicants have met the burden of enablement of a product under 35 USC 112, first paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11, 23, 31, 33, 35, 37, 38 and 42 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Amendments to the claims have obviated the basis of the specific rejections of record.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 11, 21-24, 28-31, 33-42, 46, 47 and 53 are rejected under 35 U.S.C. 102(e) for the reasons of record and for the reasons set forth below as being anticipated or clearly anticipated by Roberts (US 5,712,149).

Applicants review the subject matter encompassed by the amended claims, and point out advantages to the use of chimeric and humanized antibodies. Applicants argue that

Roberts does not teach to use chimeric or engineered antibodies as disclosed in the instant specification. See Applicants' amendment, pages 11-12. Applicants' arguments have been fully considered but not found persuasive.

As noted in the previous office actions, Roberts discloses a DNA delivery system and effector cells comprising such comprising chimeric receptors and/or cells comprising in reading frame a signal peptide component; an antibody or antigen binding fragment thereof, including spacer regions thereof comprising antibody constant- and/or hinge regions (column 6, lines 63-64; column 8, line 38 through column 9, line 51; and column 31, claims 5-6); a transmembrane component, including one from CD28 (column 8, lines 22-29) a non-naturally linked cytoplasmic signaling component of CD2 or CD28 (column. 31, cl. 1) and/or an additional non-naturally linked cytoplasmic signaling component capable of acting cooperatively wherein the cytoplasmic signaling components from CD2 and CD28 and/or others are derived from membrane spanning polypeptides or inherently comprising immunoreceptor tyrosine kinase based activation motifs (column 5, lines 36-41; column 7, line 46 through column 8, lines 14; column 32, claim 12). It is noted that MPEP 2112.01 instructs that:

> "Products of identical chemical composition can not have mutually exclusive properties.' A chemical composition and its properties are inseparable". Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re* Spada, 911 F.2d 705, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Absent evidence to the contrary, the disclosure of Roberts is presumed to anticipate the claimed subject matter in accordance with MPEP 2112.01 because it teaches limitations which anticipate

the broad limitations recited in the rejected claims. Claim 11 (ii) encompasses any 'antigen binding fragment thereof' and thus can reasonably be interpreted as encompassing any fragment of any antibody. Further, a chimeric antibody or a CDR-grafted antibody can encompass cross species modifications (humanization) and potentially have the attributes noted by Applicants, however both chimeric and CDR-grafted antibodies are simply the combination of two unrelated antibody gene sequences. The limitations noted by Applicant are not an inherent feature of these terms. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claims 11, 21-24, 28-31, 33-42, 46, 47 and 53 are rejected under 35 U.S.C. 102(e) as being anticipated or clearly anticipated by Seed *et al.* (US 5,912,170).

Applicants note that the amended claims encompass the use of chimeric and CDR-grafted antibodies. Further, Applicants point out that Seed *et al.* teach multiple cytoplasmic domains, these domains are linked naturally in nature. See Applicants' amendment, pages 12-13. Applicants' arguments have been fully considered but not found persuasive.

As noted above for Roberts, the broad nature embodied by chimeric antibody, a CDR-grafted antibody or an antigen binding fragment thereof can reasonably be interpreted to encompass any antibody fragment and any combination of antibodies joined to generate a chimeric and/or CDR-grafted antibody. Further, Examiner agrees with Applicants that the

multiple domains taught by Seed *et al.* are naturally linked in nature, however the instant claims do not exclude this possible linkage. Seed *et al.* disclose a DNA delivery system and effector cells comprising a multiplicity of chimeric receptors and/or cells comprising in reading frame a signal peptide component. As set forth in the previous office action, Seed *et al.* teach an antibody or antigen binding fragment thereof, including spacer regions thereof comprising antibody constant- and/or hinge regions (column 28, lines 56 through column 29, line 62; column 41, claim 1); a transmembrane component, including one from CD28 and CD4 (column 29, line 63 through column 30, line 20; column 31, line 23 through column 32, line 18) a non-naturally linked cytoplasmic signaling component of CD2 or CD28 (column 31, claim 1) and/or an additional non-naturally linked cytoplasmic signaling components capable of acting cooperatively wherein the cytoplasmic signaling components from CD28 or those inherently comprising non-naturally linked immunoreceptor tyrosine kinase based activation motifs (Figure 1A; column 6, line 59 through column 7, line 26; column 7, line 60 through column 8, line 4; 8, lines 29-33; column 31, lines 54-65; column 31, line 66 through column 32, line 7). Seed *et al.* further discloses the construction of use of vaccinia virus recombinants as carriers to deliver into effector cells (column 26, line 23 through column 27, line 51). In view of the broad limitations encompassed by the terms recited in the claims, the teachings of Seed *et al.* anticipate the present claims.

Claims 11, 21-24, 28-31, 33-38, 46, 47 and 53 are rejected under 35 U.S.C. 102(a) as being anticipated or clearly anticipated by Capon *et al.* (WO 96/24671).

Applicants note that the claims have been amended to recite and encompass the binding of only one component on the target cell, wherein Capon *et al.* teaches multiple domains. See Applicants' amendment, pages 13-14. Applicants' arguments have been fully considered but not found persuasive.

Examiner notes that the claims as amended cncompass DNA construct coding for a chimeric receptor which binds a cell surface antigen on a target cell (see first portion of claim 11), however, though the multi specific binding domain of Capon *et al.* comprises at least two extracellular domains, they serve to bind 'at least one specific inducer molecule' (see summary in abstract). Clearly, the teachings of Capon *et al.* is directed to the targeting of the delivery system to a particular cell. As a means to accomplish this Capon *et al.* discloses a DNA delivery system and effector cells comprising such comprising chimeric receptors and/or cells comprising in reading frame a signal peptide component; multiple antibody or antigen binding fragments, including spacer regions thereof comprising antibody constant- and/or hinge regions (page 11, line 6 through page 19, line 24; pages 36-43); transmembrane components, including ones derived from the parts of the alpha, beta or zeta chains of the T cell receptor (page 24, lines 14-17); non-naturally linked cytoplasmic signaling components of CD2 or CD28 and/or an additional non-naturally linked cytoplasmic signaling component capable of acting cooperatively

wherein the cytoplasmic signaling components from CD2 and CD28 and/or others are derived from membrane spanning polypeptides or inherently comprising immunoreceptor tyrosine kinase based activation motifs (pages. 21-22). Capon *et al.* further discloses carriers for delivering the recombinant DNAs comprising viral and non-viral vectors, liposomal vectors (page 28, lines 11-21) and effector cells comprising one or more of the above DNAs (page 29, lines 5-19). A review of the instant disclosure and that of Capon *et al.* indicates that each give similar guidance and teachings in assembly of the various components to arrive at a functional molecule. Though Capon *et al.* does indicate the potential multi specificity of binding region, clearly the targeting and binding is directed to a single cell surface antigen.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist Pauline Farrier whose telephone number is (703)305-3550.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Woitach

Art Unit 1632